

AMENDMENTS TO THE CLAIMS

The following listing of claims replaces all prior listings and versions of claims in this application.

Claims 1. to 87. (Cancelled)

88. (Currently Amended) A method for rapid crystallization of biomolecules, comprising:

- (a) providing at least one biomolecules species;
- (b) providing at least one crystallization reactor comprising an isoelectric focusing buffer having a pH range, the pH range encompassing the pI of the at least one biomolecule species;
- (c) bringing said at least one biomolecule species into contact with the at least one crystallization reactor;
- (d) introducing an electric field at said at least one crystallization reactor thereby generating a concentrated solution of said at least one biomolecule species; and
- (e) obtaining at least one crystal within said at least one crystallization reactor;

wherein the electric field is within the range of 50 - 2,000 V/cm.

89. (Previously Presented) The method according to claim 88, wherein step (c) further comprises depositing the at least one crystallization reactor and the at least one biomolecule species in running buffer.

90. (Previously Presented) The method according to claim 88, wherein step (e) further comprises extracting a biomolecule crystal from said at least one crystallization reactor.

91. (Currently Amended) The method according to claim 88, wherein ~~the electric field is within the range of 50 - 2,000 V/cm and the~~ crystallization occurs within less than 12 hours.

92. (Currently Amended) The method according to claim 88, wherein the at least one biomolecule species is selected from the group consisting of peptides, proteins, glycoproteins, polypeptides, enzymes, antibodies, protein-DNA complexes, protein complexes comprising chemical entities, polynucleotides, DNA, RNA, antigens, antigenic epitopes and variants thereof, hormones, carbohydrates, lipids, phospholipids and biotinylated probes.

93. (Previously Presented) The method according to claim 92, wherein the biomolecule species is a protein.

94. (Previously Presented) The method according to claim 93, wherein the protein is recombinant.

95. (Currently Amended) A ~~The method according to claim 88 for rapid crystallization of biomolecules, comprising:~~

(a) providing at least one biomolecules species;

(b) providing at least one crystallization reactor comprising an isoelectric focusing buffer having a pH range, the pH range encompassing the pI of the at least one biomolecule species;

(c) bringing said at least one biomolecule species into contact with the at least one crystallization reactor;

(d) introducing an electric field at said at least one crystallization reactor thereby generating a concentrated solution of said at least one biomolecule species; and

(e) obtaining at least one crystal within said at least one crystallization reactor;

wherein the at least one biomolecule species in step (a) is immobilized onto a substrate comprising a porous web material.

96. (Previously Presented) The method according to claim 88, wherein the at least one crystallization reactor is provided within a capillary.

97. (Currently Amended) A The method according to claim 88 for rapid crystallization of biomolecules, comprising:

- (a) providing at least one biomolecules species;
- (b) providing at least one crystallization reactor comprising an isoelectric focusing buffer having a pH range, the pH range encompassing the pI of the at least one biomolecule species;
- (c) bringing said at least one biomolecule species into contact with the at least one crystallization reactor;
- (d) introducing an electric field at said at least one crystallization reactor thereby generating a concentrated solution of said at least one biomolecule species; and
- (e) obtaining at least one crystal within said at least one crystallization reactor;

wherein the at least one crystallization reaction is linked, joined, or substantially contiguous to a solid substrate comprising a porous web material.

98. (Previously Presented) The method according to claim 88, wherein the isoelectric focusing buffer further comprises a polymer.

99. (Previously Presented) The method according to claim 98, wherein the polymer is selected from the group consisting of: linear polymers, branched polymers, polyacrylamide, agarose, hydrogels, cellulose, modified cellulose, cross-linked polyvinyl alcohol, cross-linked polyethylene oxide and glycol polymer.

100. (Previously Presented) The method according to claim 88, wherein the isoelectric focusing buffer has a pH range of no more than 0.2 pH units.

101. (Previously Presented) The method according to claim 88, wherein in step (b) a plurality of crystallization reactors is provided, each crystallization reactor comprising an isoelectric focusing buffer.

102. (Previously Presented) The method according to claim 101, wherein a distinct protein species is crystallized in each crystallization reactor and wherein each distinct protein species has a distinct isoelectric point.

103. (Previously Presented) The method according to claim 101, wherein the isoelectric focusing buffers in the plurality of crystallization reactors are different from one another.

104. (Previously Presented) The method according to claim 101, wherein the crystallization reactors are isolated from one another.

105. (Previously Presented) The method according to claim 101, wherein the plurality of crystallization reactors are linked, joined, or substantially contiguous to a substrate.

106. (Previously Presented) The method according to claim 88, wherein the crystallization reactor is selected from the group consisting of: immobilized pH gradient strips, pH membranes and pre-cast gels.

107. (Previously Presented) The method according to claim 88, further comprising prior to step (a) the step of sorting a solution comprising at least one biomolecule species.

108. (Previously Presented) A method for sorting a solution comprising a plurality of biomolecules and rapidly crystallizing at least one biomolecule species, comprising:

(a) providing a medium comprising a plurality of biomolecules;

(b) sorting the plurality of biomolecules on a substrate, thereby obtaining at least one locus on the substrate comprising at least one biomolecule species;

(c) recovering a portion from said substrate, the portion comprising the at least one locus;

(d) providing at least one crystallization reactor comprising an isoelectric focusing buffer having a pH range, the pH range encompassing the pI of the at least one biomolecule;

(e) bringing the portion of (c) into contact with the at least one crystallization reactor;

(f) introducing an electric field at the at least one crystallization reactor thereby generating within said at least one crystallization reactor a concentrated solution of said at least one biomolecule species; and

(g) obtaining at least one crystal within said at least one crystallization reactor of (f).

109. (Previously Presented) The method according to claim 108, wherein step (b) is carried out by a method selected from the group consisting of: isoelectric focusing, thin layer chromatography, including High Performance Liquid Chromatography (HPLC) techniques, and gel electrophoresis.

110. (Previously Presented) The method according to claim 109, wherein the method is performed under non-denaturing conditions.

111. (Previously Presented) The method according to claim 108, wherein sorting in step (b) is by the mass of the at least one biomolecule species.

112. (Previously Presented) The method according to claim 108, wherein step (e) further comprises depositing said portion and the at least one crystallization reactor in running buffer.

113. (Previously Presented) The method according to claims 108, wherein the at least one biomolecule species is a protein.

114. (Previously Presented) The method according to claim 108, wherein the electric field is within the range of 50 - 2,000 V/cm and the crystals are obtained within less than 12 hours.

115. (Previously Presented) The method according to claim 108, wherein the isoelectric focusing buffer comprises a polymer selected from the group consisting of:

polyacrylamide, agarose, hydrogels, cellulose, nitrocellulose, modified cellulose, cross-linked polyvinyl alcohol, cross-linked polyethylene oxide and glycol polymer.

116. (Previously Presented) The method according to claim 108, wherein the substrate in step (b) is a gel.

117. (Previously Presented) The method according to claim 108, wherein in step (d) a plurality of crystallization reactors comprising a plurality of isoelectric focusing buffers is provided, each isoelectric focusing buffer establishing a pH range, wherein at least one isoelectric focusing buffer establishes a pH range encompassing the pI of the at least one biomolecule.

118. (Previously Presented) The method according to claim 117, wherein each isoelectric focusing buffer comprises a polymer.

119. (Previously Presented). The method according to claim 117, wherein the plurality of crystallization reactors are isolated from one another.

120. (Previously Presented) The method according to claim 117, wherein the plurality of crystallization reactors are linked, joined, or substantially contiguous to a substrate comprising a porous web material.

121. (Previously Presented) The method according to claim 108, wherein the crystallization reactor is selected from the group consisting of: immobilized pH gradient strips, pH membranes and pre-cast gels.

122. (Currently Amended) An apparatus suitable for inducing rapid formation of biomolecule crystals, comprising:

(a) a buffer chamber having an upper side and a lower side, the lower side being sealed with a bottom such that the buffer chamber encloses at least one buffer compartment capable of holding fluids;

(b) at least one crystallization reactor contained within said buffer chamber, the at least one crystallization reactor comprising an isoelectric focusing buffer;

(c) a device for generating an electrical field;

(d) two salt bridges having two ends, one end of each salt bridge being in contact with one end of the holder and one end of each salt bridge being contained within the at least one buffer chamber; and, optionally,

(d)(e) means for circulating fluids contained within the at least one buffer compartment.

123. (Previously Presented) The apparatus according to claim 122, wherein component (b) is a holder having two ends, an upper side and a lower side, the holder encompasses at least one crystallization reactor, the at least one crystallization reactor comprising an isoelectric focusing buffer, wherein the holder is contained within the buffer compartment.

124. (Canceled)

125. (Currently Amended) The apparatus according to claim ~~[[124]]~~ 122, comprising two buffer chambers, each buffer chamber enclosing one end of one salt bridge.

126. (Previously Presented) The apparatus according to claim 122, further comprising a temperature-controlled module enabling to manage the temperature at the at least one crystallization reactor.

127. (Previously Presented) The apparatus according to claim 122, wherein component (b) comprises a holder adapted for supporting a substrate and comprising at least one crystallization reactor.

128. (Previously Presented) The apparatus according to claim 127, wherein the holder is a capillary adapted for comprising at least one crystallization reactor.

129. (Previously Presented) The apparatus according to claim 127, wherein the holder encompasses at least one cavity wherein the at least one cavity is adapted for containing a crystallization reactor.

130. (Previously Presented) The apparatus according to claim 129, wherein the crystallization reactor is selected from the group consisting of: immobilized pH gradient strips, ph membranes and pre-cast gels.

131. (Previously Presented) The apparatus according to claim 122, wherein the buffer chamber comprises a non-conductive material.

132. (Previously Presented) The apparatus to claim 127, wherein the holder comprises a material having a larger resistance than that of the polymer comprised within the crystallization reactor.

133. (Previously Presented) The apparatus according to claim 131, wherein the non-conductive material is selected from the group consisting of: poly-N-methyl methacrylamide, acrylic, lucite, polystyrene, ceramic, glass and poly-methyl-methacrylate.

134. (Previously Presented) The apparatus according to claim 127, wherein the holder comprises a material that is impermeable to biomolecules.

135. (Previously Presented) The apparatus according to claim 122, wherein the device for generating an electrical field comprises a plurality of electrodes.

136. (Previously Presented) The apparatus according to claim 135, wherein the plurality of electrodes comprises a metal selected from the group consisting of: platinum, titanium, chromium, gold, tantalum, palladium, palladium oxide, germanium, nickel and rhodium or alloys comprising same.

137. (Previously Presented) The apparatus according to claim 122, wherein the device for generating an electrical field supplies DC or AC currents and generates an electric field within the range of 50 - 2,000 V/cm.

138. (Previously Presented) The apparatus according to claim 122, wherein the buffer compartment is adapted for holding a solution comprising running buffer and at least one biomolecule dissolved with the running buffer.

139. (Previously Presented) The apparatus according to claim 122, further being automated.

140. (Currently Amended) The apparatus according to claim 122, wherein the biomolecule is selected from the group consisting of: peptides, proteins, glycoproteins, polypeptides, enzymes, antibodies, protein-DNA complexes, protein complexes comprising chemical entities, polynucleotides, DNA, RNA, antigens,

antigenic epitopes and variants thereof, hormones, carbohydrates, lipids, phospholipids and biotinylated probes.

141. (Previously Presented) The apparatus according to claim 140, wherein the biomolecule is a protein.

142. (Currently Amended) The apparatus according to [[of]] claim 122, wherein crystallization occurs within less than 12 hours.

143. (New) The apparatus according to claim 135, comprising two buffer chambers, each buffer chamber enclosing one electrode.